UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/593,071	01/19/2007	Catherine Rougeot	296415US0PCT	6477

22850 7590 08/05/2009

OBLON, SPIVAK, MCCLELLAND MAIER & NEUSTADT, P.C.
1940 DUKE STREET
ALEXANDRIA, VA 22314

EXAMINER
JIANG, DONG

ART UNIT	PAPER NUMBER
1646	

NOTIFICATION DATE	DELIVERY MODE
08/05/2009	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

patentdocket@oblon.com
oblonpat@oblon.com
jgardner@oblon.com

Office Action Summary	Application No.	Applicant(s)	
	10/593,071	ROUGEOT ET AL.	
	Examiner	Art Unit	
	DONG JIANG	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 April 2009*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-66* is/are pending in the application.

4a) Of the above claim(s) *10-14,17-19,22-64 and 66* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-9,15,16,20,21 and 65* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-66* are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 September 2006* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/24/06*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED OFFICE ACTION

Applicant's election with traverse of Group I invention, claims 1-19, 15, 16, 20, 21 and 65, filed on 10 April 2009 is acknowledged. The traversal is on the ground(s) that the Examiner has not considered that the claims in each group are considered to have related inventions under 37 C.F.R. § 1.475(b) in which the inventions are considered to have unity of invention; that while Rule 13.1 and 13.2 are applicable 37 C.F.R. § 1.475(b) provides in relevant part that "a national stage application containing claims to different categories of invention are considered to have unity of invention if the claims are drawn to ...(3) a product, process especially adapted for the manufacture of said product and a method of using said product..."; and that a search of all the claims would not impose a serious burden on the Office. This is not found persuasive because the "special technical features" regarding unity required by Rule 13.1 and 13.2 shall mean those technical features that define a contribution which each of the claimed inventions, considered as a whole, makes over the prior art, which is not the case in the instant situation. As clearly addressed in the last Office Action, the shared technical feature of BPLP or a peptide derivative of thereof is not a special technical feature as it does not make a contribution over the prior art in view of Dickinson et al. (Current Eye Research 15:377-386, 1996), which teaches a BPLP peptide comprising the amino acid sequence of SEQ ID NO:3. Therefore, the groups lack unity of invention. Further, a search of all the claims would impose a serious burden because they require separate searches of the art.

The requirement is still deemed proper and is therefore made FINAL.

Currently, claims 1-66 are pending, and claims 1-9, 15, 16, 20, 21 and 65 are under consideration. Claims 10-14, 17-19, 22-64 and 66 are withdrawn from further consideration as being drawn to a non-elected invention.

Formal Matters:

Information Disclosure Statement

Applicant's IDS submitted on 10/24/06 is acknowledged and has been considered. A signed copy is attached hereto.

Priority acknowledgement

This application is a national stage entry (371) of PCT/IB05/000700 with the international filing date of 3/18/05, which is acknowledged.

Specification

The specification is objected to for the following informalities, and appropriate correction is required for each item:

On page 8, lines 12-13, it recites "through clivage of the BPLP protein precursor by natural maturases …". It seems that the word "clivage" should be "cleavage".

Claims

Claims 1 and 4-9 are objected to for the following informalities, and appropriate correction is required for each item:

Claim 1 recites "the Basic Prolin-rich …" in line 1, which should be "the Basic Proline-rich …".

Claim 4-9 recite "SEQ ID No:". The correct way is "SEQ ID NO:"

Rejections under 35 U.S.C. §112:

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-9, 15, 16, 20, 21 and 65 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite for the recitation "a maturation product" because it is unclear what the term encompasses, and whether it is one product with specific sequence structure, or more than one product with different sequence structures. A "definition" of the term is noted in the specification, which states "[A] 'maturation product' is a peptide that is obtained through cleavage of the BPLP protein precursor by natural maturases or prohormone converting enzymes, or related mono or paired basic amino acid-cleaving enzymes *such as* furin, PC convertases or PACE 4 (Seidah, 1995),

for example" (page 8, lines 12-15). However, such "definition" is merely exemplary, which falls within the *intended* definition, but is not considered, in itself, to provide definitive structural limitation for the claimed peptide. The claim is further indefinite for the recitation "a peptide derivative" for the similar reasons. On page 8 of the specification, it states "[T]he 'peptides derivatives' are peptides having amino acid substitutions from a parent peptide, *preferably* from one to two …" (lines 17-21). Once again, such language falls within the *intended* definition. The metes and bounds of the claim (the structure of the claimed peptide), therefore, cannot be determined. MPEP (2171) makes it clear that the claims must particularly point out and distinctly define the metes and bounds of the subject matter that will be protected by the patent grant, which is not dependent on the views of applicant or any particular individual, but is evaluated in the context of whether the claim is definite, i.e., whether the scope of the claim is clear to a hypothetical person possessing the ordinary level of skill in the pertinent art. The claim is further indefinite for the recitation "a modulatory property" because it is unclear what it is meant. Further, the claim recites the limitation "*the* Basic Prolin-rich …" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 2 is similarly indefinite for the recitation "peptide derivative".

Claims 15 and 16 are similarly indefinite for the recitation "a derivative" and "mimetic".

Claim 4 is indefinite because it is unclear what X2 would be if X1 is Cys.

The remaining claims are included in this rejection because they are dependent from the specifically mentioned claims without resolving the indefiniteness issue belonging thereto.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 21 and 65 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention.

The factors considered when determining if the disclosure satisfies the enablement requirement and whether any necessary experimentation is "undue" include, but are not limited to: 1) nature of the invention, 2) state of the prior art, 3) relative skill of those in the art, 4) level

of predictability in the art, 5) existence of working examples, 6) breadth of claims, 7) amount of direction or guidance by the inventor, and 8) quantity of experimentation needed to make or use the invention. *In re Wands*, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

Claims 21 and 65 encompass a second pharmaceutical agent acting synergistically with BPLP-peptide, wherein no structural limitation is required for or associated with the second agent. The specification does not disclose any "second pharmaceutical agent" meeting the limitation of the claims. The specification provides no guidance or working example as to how to make such an agent. The prior art has not established such agents. As there is no structural limitation is associated with the agent, there is no way for a skilled artisan to predict the structure of such an agent, based on which said agent could be made. Therefore, it would require undue experimentation to practice the claimed invention.

Due to the large quantity of experimentation necessary to find and determine the structure of encompassed agents in order to make the agents, and possibly make and screen same for activity, the lack of direction/guidance presented in the specification regarding structural features required in order to provide activity, the absence of working examples directed to same, the complex nature of the invention, the total lack of predictability of the structure of the agents, and the breadth of the claims which embraces a broad and diverse class of structural molecule, and fails to recite any structural limitation, undue experimentation would be required of the skilled artisan to make the claimed invention.

Claims 1-3, 15, 16, 20, 21 and 65 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 1-3, 15, 16 and 21 are directed to [encompass] a peptide that is a maturation product of a BPLP or a peptide derivative or a mimetic thereof, wherein the peptide derivative exhibits a modulatory property, which reads on a functional equivalent of a BPLP with or without structural similarity. Thus, the claims are drawn to a genus of peptides that are maturation products of a BPLP, and a genus of peptide derivatives that are defined only by functional limitation. Claims 20 and 65 encompass "a BPLP protein", which reads on any or all

known and unknown BPLP proteins. Claims 21 and 65 further comprise a second pharmaceutical agent acting synergistically with BPLP-peptide, wherein no structural limitation is required for or associated with the second agent.

With respect to claims 1-3, 15, 16 and 21, the specification merely discloses *one* peptide that is assumed to be derived from the human BPLP (page 5, lines 24-26), or a maturation product of a human salivary sialorphin-like peptide (page 45, lines 8-14), wherein the peptide consists of SEQ ID NO:3, and has inhibitory potency towards a human ectoendopeptidease (page 46, Table). In addition, the specification teaches five peptide derivatives of SEQ ID NO:3, and they are SEQ ID NO:4, 5, 7, and the last two in the Table on page 46. However, *only* peptide of SEQ ID NO:4 showed comparable potency towards a human and rat ectoendopeptideases as that of peptide of SEQ ID NO:3 (page 46, Table, and lines 8-14), and SEQ ID NO:5 and 7 do not seem ever being tested. Thus, only *one* molecule from each claimed genus (a peptide of maturation product of a BPLP (SEQ ID NO:3), and a peptide derivative thereof (SEQ ID NO:4)) meeting the limitation of the claims was ever identified. No other peptide molecules meeting the limitation of the claims were ever identified or particularly described. With respect to claims 20 and 65, the specification merely disclosed one BPLP, the human BPLP of SEQ ID NO:2, and no other BPLP meeting the limitation of the claim were ever identified or particularly described. With respect to claims 21 and 65, the specification does not disclose *any* "second pharmaceutical agent" meeting the limitation of the claims, i.e., an agent that acts synergistically with BPLP-peptide.

To provide adequate written description and evidence of possession of a claimed genus, the specification must provide sufficient distinguishing identifying characteristics of the genus. The factors to be considered include disclosure of compete or partial structure, physical and/or chemical properties, functional characteristics, structure/function correlation, methods of making the claimed product, or any combination thereof. In this case, the only factor present in the claims is a functional characteristic (for "peptide derivative"), a modulatory property against a metallo-ectopeptidase. There is no structural identification for the encompassed peptide derivative. Thus, with the exception of the peptides of SEQ ID NO:3 and 4, and the human BPLP of SEQ ID NO:2, the skilled artisan cannot envision the detailed chemical structure of the encompassed "peptide derivative", "mimetic of a peptide" (claims 1-3, 15, 16 and 21, for

example), "a BPLP protein" (claim 20, for example), and the "second pharmaceutical agent" (claims 21 and 65); and therefore conception is not achieved regardless of the complexity or simplicity of the method of making a peptide. Accordingly, the specification does not provide adequate written description of the claimed genus.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116).

Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolating it. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016. One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Therefore, in the instant case, only the peptides of SEQ ID NO:3 and 4, and the human BPLP of SEQ ID NO:2, but not the full breadth of the claims ("peptide derivative", "mimetic of a peptide", "a BPLP protein", and the "second pharmaceutical agent") meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

Rejections Over Prior Art:

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-4, 6, 15, 16 and 20 are rejected under 35 U.S.C. 102(b) as being anticipated by Dickinson et al. (Curr Eye Res. 1996 Apr;15(4):377-86, provided by applicants).

Dickinson teaches a human BPLP peptide, wherein the amino acid sequence of the BPLP pre-proprotein (Figure 1, and page 379, 2nd column, the last line) is 100% identical to the present SEQ ID NO:2. Additionally, Dickinson teaches that the BPLP is a human tear protein (abstract), and the polypeptide consists of a 21 residue hydrophobic secretory peptide leader sequence, and a 180 residue secreted peptide (page 379, 1st column, 3rd paragraph, and Figure 2A), indicating a mature form of the BPLP. Therefore, the reference anticipates claims 1-4 and 6, as Dickinson's mature form of the BPLP is a maturation product of the BPLP, and comprises the presently claimed sequences such as SEQ ID NO:3. Note, with respect to the functional limitations in claims 2 and 3, they would be inherent property of Dickinson's mature BPLP since it meets the structural limitation of the claims. With respect to claims 15, 16 and 20, dissolving solutions, such as water or buffers would meet the limitation as being "a pharmaceutically acceptable carrier". Thus, in view of Dickinson's disclosure, one of ordinary skill in the art would consider that Gorman is in possession of such a composition. Therefore, the reference also anticipates claims 15, 16 and 20.

Conclusion:

No claim is allowed.

Advisory Information:

Any inquiry concerning this communication should be directed to Examiner Dong Jiang whose telephone number is 571-272-0872. The examiner can normally be reached on Monday - Friday from 9:30 AM to 7:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol, can be reached on 571-272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Dong Jiang/
Primary Examiner, Art Unit 1646
7/30/09